Safe prescribing of tacrolimus

Tacrolimus has been the basis of immunosuppression in both kidney and liver transplant patients in our units for well over a decade. It is more potent than ciclosporin and has better outcome data, but this potency also extends to its toxicity. Tacrolimus is a narrow-therapeutic range nephrotoxic medication with a small gap between subtherapeutic and toxic levels. The target range for a particular indication or patient may not be that as detailed as standard on ICE.

Brand-name prescribing
We keep four brands of tacrolimus. Adoport and Prograf are licensed for twice-daily dosing, and Advagraf and Envarsus for once-daily administration. NONE of these brands is freely interchangeable with another without careful plasma-level monitoring. EPMA requires a brand to be specified but clinic letters and hand-written prescriptions might not. An MHRA warning exists about the need to prescribe by brand.

https://www.gov.uk/drug-safety-update/oral-tacrolimus-products-prescribe-and-dispense-by-brand-name-only-to-minimise-the-risk-of-inadvertent-switching-between-products-which-has-been-associated-with-reports-of-toxicity-and-graft-rejection

Drug interactions with tacrolimus
Tacrolimus dosing and levels do not depend on renal function, but many medicines interact with tacrolimus by affecting metabolic processes that are responsible for handling and clearing the drug. Common examples that can be dangerous include enzyme inhibitors such as clarithromycin and fluconazole. Many other potential interacting medications exist and it is safest to check or seek advice before adding any medication. Grapefruit juice, NSAIDs and herbal medicines should also be avoided. documented: St John's Wort for example is a known enzyme inducer, but in general potential herbal medicine interactions are less well investigated and documented. Strangely, tacrolimus levels can also be increased by concurrent diarrhoea and this may require dose reduction (and dose increasing again as diarrhoea resolves).

Parenteral dosing
The dosing of tacrolimus recommended in the SPC and BNF is likely to result in tacrolimus concentrations significantly above those we would aim for. Most UK renal units therefore administer tacrolimus intravenously, over 24 hours, at ONE-FIFTH of the total daily oral dose initially. Full information can be found on the Trust renal transplant immunosuppression policy on the Intranet "Policy and Patient Leaflets" link.

Full support can be obtained from the Renal Transplant Teams or any pharmacist.

Agreed by: Andrew Davison Version 1.0
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